

### REMARKS

Claims 1-17, 20-26, and 28-31 are pending. Applicants have cancelled claims 20-26 without prejudice and added new claim 32. Claims 1-17 and 28-32 will therefore be pending and under examination upon entry of the proposed amendments.

Applicants have replaced "R1" in claims 1, 9-15, 28, 31, and 32 with "R," as suggested by the Examiner. Applicants have deleted the phrase "prodrug or solvate" in claims 1, 16, 17, and 28.

Claim 28 has been further amended as follows. Applicants have deleted the phrase "an appropriate" and amended lines 9 and 10 of claim 28 to read "converting the compound obtained into a further compound of formula (I) as claimed in claim 1" instead of "converting the compound obtained into a further compound according to the invention."

New claim 32 depends from claim 28 and is directed to a process in which "the mixed anhydride is prepared from reaction of formic acid and acetic anhydride." Support for this amendment can be found throughout the specification, e.g., page 14, lines 1-2.

Finally Applicants have amended the title as required by the Examiner.

No new matter is introduced by these amendments, which are made for the sole purpose of expediting prosecution of the present application. Applicants reserve the right to pursue any cancelled subject matter in one or more later filed continuing applications.

#### Rejections under 35 U.S.C. § 112, first paragraph

I. Claims 1-17, 20-26, and 28 are rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph because "the specification does not reasonably provide enablement for making prodrugs or solvates of the claimed compounds" (Office Action, page 2).

The rejection of claims 20-26 is moot in view of the cancellation of these claims.

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have deleted the phrase "prodrug or solvate" in claims 1, 16, 17, and 28.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

II. Claim 11 is rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. The rejection states, in part:

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compounds to treat a disease condition mediated by collagenase 3, an obstructive airways disease, osteoarthritis, atherosclerosis, a metalloproteinase mediated disease condition or rheumatoid arthritis with a therapeutically-effective amount of a compound of claim 1 or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

While not agreeing with the ground for rejection, Applicants believe, based on the above-stated ground for rejection, that claims 20-26 were intended and not claim 11. For the sole purpose of expediting prosecution of the present application, Applicants have cancelled claims 20-26. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 9, and 28 are rejected under 35 U.S.C. § 112, second paragraph on various grounds for allegedly being indefinite. Each of the stated grounds for rejection (a)-(e) are considered in turn.

(a) Claim 1 is rejected because formula (I) recites "R<sub>1</sub>" and the remainder of the body of claim 1 recites "R<sub>1</sub>." Applicants have replaced "R<sub>1</sub>" in claims 1, 9-14, 28, 31, and 32 with "R<sub>1</sub>" as suggested by the Examiner. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

(b) Applicants have added a period at the end of claim 9 and respectfully request reconsideration and withdrawal of the rejection of claim 9.

(c)-(e) Claim 28 is rejected because of the recitation of "an appropriate mixed anhydride" and "converting the compound obtained into a further compound according to the invention."

Applicants respectfully disagree with the grounds for the rejection; however to expedite prosecution, Applicants have deleted the phrase “an appropriate” in claim 28. Claim 28 is directed to a process for preparing a compound of formula (I) as claimed in claim 1. Such compounds contain a formylated hydroxyamino group, i.e., -N(CHO)(OH). The process includes *inter alia* converting a compound of formula (IV), which contains a hydroxyamino group, i.e., -NH(OH), to a compound of formula (I) by formylation with a mixed anhydride. Formylation is a term of art in organic chemistry that refers to a reaction in which a compound is functionalized with a formyl group, i.e., -CHO. The skilled artisan would understand which mixed anhydrides could be used for formylation and which could not. Accordingly, the skilled artisan, guided by his or her skill in the art and/or the specification, would understand the metes and bounds of “mixed anhydride.”

In addition, and for the sole purpose of expediting prosecution of the present application, Applicants have amended lines 9 and 10 of claim 28 to read “converting the compound obtained into a further compound of formula (I) as claimed in claim 1” instead of “converting the compound obtained into a further compound according to the invention” to further clarify that the “further compound” is a compound encompassed by formula (I) in claim 1.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of each of the above 35 U.S.C. § 112, second paragraph rejections.

Rejection under 35 U.S.C. § 103

Claims 1-3, 8-11, 14, 16-17, and 23-26 are rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Barlaam, et. al., U.S. Patent 6,734,184 (Barlaam). This is respectfully traversed.

The Office has indicated that claims 29-31 are “patentable” (Office Action, page 15) over Barlaam. More specifically, the Office states (Office Action, page 15, emphasis added):

Claims 29-31 are patentable over Barlaam, et. al., U.S. Patent No. 6,734,184, which teaches arylpiperazine compounds as metalloproteinase inhibiting agents. The difference between the compounds of the closest prior art and the instant compounds is that the instant compounds require the presence of R2 substituted with ‘one or more fluorine groups,’ which is neither taught nor suggested by the reference. Therefore, the claims are free of prior art.

Independent Claim 1, however, also requires “the presence of R2 substituted with ‘one or more fluorine groups.’” More specifically, claim 1 recites (emphasis added):

R2 represents a group selected from C1-6 alkyl or aryl, which said group is substituted by one or more fluorine groups

Thus, Applicants submit that claim 1 is patentable over Barlaam for at least the reason stated by the Office in connection with present claims 29-31 (i.e., “[t]he difference between the compounds of the closest prior art and the instant compounds is that the instant compounds require the presence of R2 substituted with ‘one or more fluorine groups,’ which is neither taught nor suggested by the reference”). Since claims 2, 3, 8-11, 14, 16, and 17 depend from claim 1, these claims are also patentable over Barlaam for at least this same reason.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Applicants submit that all claims are in condition for allowance.

The fee in the amount of \$460 for the two month extension fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of a Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 06275-487US1 / 100985-1P US.

Respectfully submitted,

Date:

June 25, 2008

John T. Kendall  
John T. Kendall, Ph.D.  
Reg. No. 50,680

Fish & Richardson P.C.  
225 Franklin Street  
Boston, MA 02110  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906